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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,827	08/16/2007	Bernhardt L. Trout	MTV-073.01	1437

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FOLEY HOAG, LLP
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EXAMINER

GUDIBANDE, SATYANARAYAN R

ART UNIT	PAPER NUMBER
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1654

NOTIFICATION DATE	DELIVERY MODE
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03/01/2011

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patent@foleyhoag.com

Office Action Summary	Application No. 10/590,827	Applicant(s) TROUT ET AL.	
	Examiner SATYANARAYANA R. GUDIBANDE	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-76 is/are pending in the application.
- 4a) Of the above claim(s) 1-47 and 57-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>07/02/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of claims 48-56 and election of formula IX as species wherein the variable R is H, R' is a side chain of arginine and X is O in the reply filed on 1/24/11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants acknowledge that claims 48-56 had not been placed in any group as they were notified as belonging to a non-statutory group due to improper multiple dependent claims. If they had been presented in the proper format, the claims 48-56 would have been placed in group IX in office action dated 10/6/10. Accordingly claims 48-56 has been placed in the group IX.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. In the instant application, several patent and non-patent literature references have been cited throughout the specification, especially in pages 39-41, 46-49, 53-55 and 59-61. Neither the references have been listed on IDS nor copies of the same have been submitted for consideration.

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Status of pending claims

Applicant's amendment to claims in the response filed on 1/24/11 has been acknowledged.

Claims 1-76 are pending.

Claims 1-47 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/24/11.

Claims 57-76 have not been placed in any group and have been withdrawn from further consideration as they belong to the non-statutory class of improperly multiple dependent claims.

Claims 48-56 are examined on the merit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

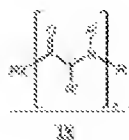
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 48 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Robinson (US 2,843,525).

In the instant application applicants claim a method suppressing or preventing aggregation of a protein in solution comprising the step of combining in a solution (i) a polymer

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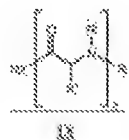
of formula IX: wherein the 'R' is 'H', R' is an alpha-amino acid wherein at least one instance 'R'' is 'arginine', 'X' is 'O' and p is an integer from 2-1000 and (ii) a protein.

The claim as recited implies that the solution comprises of two protein solutions with one of the proteins comprises of an arginine residue in it's peptide sequence.

Robinson discloses a solution of polyarginine and zinc insulin solution (column 9, Example 19). The solution comprises of polyarginine molecules that comprises of 4 or 8 or 10 to 15 arginine residues (column 1, lines 65-72), and insulin in an aqueous solution of cresol-glycerin-water, pH 3.2 and sodium phosphate, pH 7.1 (column 9, lines 50-62). This reads on instant claims 48 and 54.

2. Claims 48 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Cotten, 1986, Nucleic Acids Research, 14, 3671-3686.

In the instant application applicants claim a method suppressing or preventing aggregation of a protein in solution comprising the step of combining in a solution (i) a polymer



of formula IX: wherein the 'R' is 'H', R' is an alpha-amino acid wherein at least one instance 'R'' is 'arginine', 'X' is 'O' and p is an integer from 2-1000 and (ii) a protein.

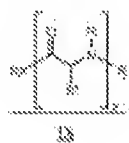
Cotton discloses a solution of histones (corresponds to protein of the instant claims) and polyarginine (MW 40,000) in the presence of novobiocin. Cotten discloses that there was a decrease in precipitation of histone in the presence of polyarginine when the solution contained

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novobiocin (page 3680). The molecular weight of 40,000 for the polyarginine corresponds to 229 residues of arginine in the polymer. This reads on the instant claims 48 and 54.

3. Claims 48, 49, 52 and 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyamoto, 2001, International Journal of Pharmaceutics, 226, 127-138.

In the instant application applicants claim a method suppressing or preventing aggregation of a protein in solution comprising the step of combining in a solution (i) a polymer



of formula IX: wherein the 'R' is 'H', R' is an alpha-amino acid wherein at least one instance 'R' is 'arginine', 'X' is 'O' and p is an integer from 2-1000 and (ii) a protein.

Miyamoto discloses an aqueous solution of recombinant human granulocyte colony-stimulating factor (rh-CSF), polyarginine and FITC dextran as being used as model water-soluble macromolecule and protein drug, respectively (page 129, column 1, paragraph 1). Miyamoto further discloses that rh-CSF solution containing poly-Arg was administered via a flexible polyurethane attached to a microsyringe (page 130, column 1, bridging paragraph from page 129). The molecular weight of Poly Arg used was 50 kDa. This corresponds to 287 residues of arginine. This reads on instant claims instant claims 48, 49, 52 and 54-56.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

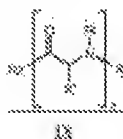
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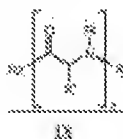
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 48-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyamoto, 2001, International Journal of Pharmaceutics, 226, 127-138.

In the instant application applicants claim a method suppressing or preventing aggregation of a protein in solution comprising the step of combining in a solution (i) a polymer



of formula IX:  wherein the 'R' is 'H', R' is an alpha-amino acid wherein at least one instance 'R' is 'arginine', 'X' is 'O' and p is an integer from 2-1000 and (ii) a protein.

Miyamoto discloses an aqueous solution of recombinant human granulocyte colony-stimulating factor (rh-CSF), polyarginine and FITC dextran as being used as model water-soluble macromolecule and protein drug, respectively (page 129, column 1, paragraph 1). Miyamoto further discloses that rh-CSF solution containing poly-Arg was administered via a flexible polyurethane attached to a microsyringe (page 130, column 1, bridging paragraph from page

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129). The molecular weight of Poly Arg used was 50 kDa. This corresponds to 287 residues of arginine. This reads on instant claims instant claims 48, 49, 52 and 54-56.

Miyamoto discloses the aqueous solution of Poly-Arg and rh-CSF for administering to rats via nasal route or for intravenous injection. It does not disclose recombinant antibody or cytokines such as interferon or EPO.

However, Miyamoto discloses that that poly-Arg can be used to provide adequate nasal adsorption of protein drugs and cytokines which have a molecular weight of about 20 kDa (page 136, column 2, paragraph 1). This further reads on instant claims 50, 51 and 53.

It would have been obvious to one of ordinary skill in the art to use the teachings of Miyamoto to arrive at the instant invention of having cytokines such as interferon or insulin in an aqueous solution along with poly-Arg. Because, Miyamoto discloses that such a combination of recombinantly produced biologically active peptide and poly-Arg in aqueous solution can be used for administering to animals. One of ordinary skill in the art would have been motivated to do so given the fact Miyamoto successfully used the method to deliver rh-CSF nasally in rats. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (In re Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); In re Bode 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie

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obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SATYANARAYANA R. GUDIBANDE/
Examiner, Art Unit 1654
/Andrew D Kosar/
Primary Examiner, Art Unit 1654